

2/23
FIG. 1B

TTGCTGATTTCCTCGAAGACTACATCGATTTTGGGATAAATGAGCCAGATCTACTTCGTC
 1261 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 1320
 A D F L E D Y I D F A I N E P D L L R P
 90 100
 CAGTAGTGATTGCTCCACAATTTTCCCGACAAATGCTCGATAGGAACTATTGCTTGGGA
 1321 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1380
 V V I A P Q F S R Q M L D R K L L L G N
 110 120
 T n2274
 ↑
 ATGTTCCAAAACAAATGACATGCTATATTCGAGAGTATCACGTGGATCGAGTGATCAAAA
 1381 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1440
 V P K Q M T C Y I R E Y H V D R V I K K
 130 140
 AGCTCGACGAGATGTGTGATTTAGGTGAGAAACTGGAAGCTCTCGTGTATTATAATC
 1441 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1500
 L D E M C D L D
 150
 TTGCTTAAACTTCAGACTCCTTTTTTCTGTTTCTACACGGCCGAGCTGGATCCGGAAAAT
 1501 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1560
 S F F L F L H G R A G S G K S
 160
 CAGTAATTGCATCACAAGCTCTTTTCAAATCTGACCAACTTATTGGAATGTGAGTGGTAT
 1561 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1620
 V I A S Q A L S K S D Q L I G I
 170 180
 TATCTGAATCTACGGATCTTCATTCTATTACAGAAATTATGATTCAATCGTTTGGCTCAA
 1621 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1680
 N Y D S I V W L K
 190
 AGATAGTGAACAGCTCCAAAATCTACATTCGATTTATTTACGGATATTTTGTGTATGCT
 1681 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1740
 D S G T A P K S T F D L F T D I L L M L
 200 210
 A n1920/n2247
 ↑ Intron 3
 AAAGTGAGTGAATAGAGTGATGTAACATTCAGCATGATTTTGAAATTATGAAAATTGA
 1741 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1800
 K
 CCTGGTTAGCTTTTAATTGATATTTTCGTGACGCTTGCATGTTTTGTGTGTTGAAGACG
 1801 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1860
 AGCCCGTGTGTGAGCGACACGGATGACTCGCATTGATCACCAGCTTCATTAACCGTGT
 1861 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1920
 A n2273
 ↑
 TCTTTCAAGAAGCGAAGACGATCTTCTCAATTTCCCATCGGTGGAGCATGTCACGTCAGT
 1921 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1980
 S E D D L L N F P S V E H V T S V
 220

Title: CLONING, SEQUENCING AND CHARACTERIZATION
 OF TWO CELL DEATH GENES AND USES THEREFOR
 Applicant (s): H. Robert Horvitz et al.
 Filing Date: December 3, 1997
 Serial No.: 08/984,178
 Customer No.: 21559
 Page 2 of 23

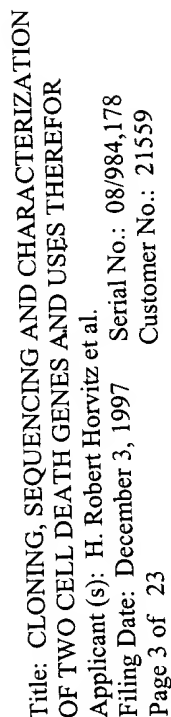


FIG. 1C

Intron 4

1981 TGTACTCAAAAGGATGTAAGTTGCTTGCCGATTCTGGTACAATATCTTAAATTATTGGT 2040
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
V L K R M

230
TTTTAGATCTGCAACGCACTCATTGATCGTCCAAATACCTTTATTTCGTATTGATGACGTA
2041 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2100
I C N A L I D R P N T L F V F D D V
240 250

A n1948 T n1947
↑ ↑
GTTCAAGAAGAAAACAATTCGTTGGGCTCAGGAGCTACGTCTTCGATGTCTTGTAACACT
2101 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2160
V Q E E T I R W A Q E L R L R C L V T T
260 270
CGTGACGTGGAAATATCAAATGCTGCTTCTCAAACATGCGAATTCATTGAAGTGACATCA
2161 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2220
R D V E I S N A A S Q T C E F I E V T S
280 290
TTGGAATCGATGAATGTTATGATTTTCTAGAAGCTTATGGAATGCCGATGCCTGTTGGA
2221 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2280
L E I D E C Y D F L E A Y G M P M P V G
300 310
Tc4 n1416
↓
GAAAAAGAAGAAGATGTGCTTAATAAAACAATCGAACTAAGCAGTGGAATCCAGCAACG
2281 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2340
E K E E D V L N K T I E L S S G N P A T
320 330

Intron 5

CTTATGATGTTTTTCAAGTCTTGTGAACCGAAAAACATTTGAAAAGTGAGTGGGACATACC
2341 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2400
L M M F F K S C E P K T F E K
330
AATTTGAGACTTTTTAAATAATTTATTCTACAATAAAAGTTAATCAAAAAGTTTCATAGC
2401 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2460
TGATTGTCTTTAAATTTTACGAATTGAGGATCAAAATCAAGAATTAGGATCCTGGCACGA
2461 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2520
GAGAAAACTGTGTAGCTACCGTACCCGAGAGATTTTCTTGATATTTGCCATCGATTTAAT
2520 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2580
TTTTTAAGAAAATTATCGTTTTTACATAATTGAACAAGAGATACACGGTCTCGACCCGACG
2581 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2640
GAAATTTTTTAAATGAAAGCGAGTATGAGCCTGTTTTTCATTATTTTCGATTTTCTCTTG
2641 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2700
TTGTTTCTTTTATTTAAAGCCTTTTATTTTGAACAAGTCTAAAAATATTAATAAATCTGA
2701 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2760
ATAAAATATTTAAAAAAAATCAAGTAAATAGAAAAACAGCAAGGCTGGAGACTACTGTA
2760 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2820
CTTCTAAATCCGCATACTCTTTTTATTTAATCATTTTCCGGAATGTGCGAAACGAAATAA
2821 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2880
TACATTTTGTAGTCCAAAATCGCTAGGTATATTCTTAAATTTATCAACATTTTGCATTCA



4/23

FIG. 1D

2881 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2940
GAATGGCACAGCTTAATAACAAATTGGAAAGTCGAGGATTAGTCGGTGTGAATGTATCA
2941 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3000
M A Q L N N K L E S R G L V G V E C I T
340 350

3001 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3060
CCCCTTACTCGTACAAGTCACTCGCAATGGCTCTTCAAAGATGTGTTGAAGTTTGTTCAG
P Y S Y K S L A M A L Q R C V E V L S D
360 370

3061 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3120
ATGAGGATCGAAGTGCTCTTGCTTTTCGAGTTGTGATGCCTCCTGGAGTTGATATACCCG
E D R S A L A F A V V M P P G V D I P V
380 390
A n1894
↑

3121 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3180
TCAAGCTATGGTCATGTGTTATTCCAGTTGATATTTGTTCAAATGAAGAAGAACAATTGG
K L W S C V I P V D I C S N E E E Q L D
400 410

3181 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3240
ATGATGAAGTTGCGGATCGGTTGAAAAGACTCAGCAAGTATGAGTCTTGAAATTTGAAGA
D E V A D R L K R L S K
420
Intron 6

3241 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3300
TTTAAATTAACACTTAAATTTTCAGACGTGGAGCTCTTCTCAGTGGAAAACGAATGCCCG
R G A L L S G K R M P V
430 440

3301 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3360
TTTTGACATTCAAATTGATCATATTATCCATATGTTCTTGAAACACGTCGTTGATGCAC
L T F K I D H I I H M F L K H V V D A Q
450 460

3361 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3420
AAACTATCGCGTATGCTGAAAATGTCTCAACTTTCAATTAAATTTTAAATTTTCAGAAAT
T I A N
GGAATCTCAATTCTCGAGCAGCGTCTTCTTGAAATAGGAAACAATAATGTATCAGTACCG
3421 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3480
G I S I L E Q R L L E I G N N N V S V P
470 480

3481 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3540
GAGCGACATATACCATCACATTTCCAAAAATTCGTCGTTTCATCAGCCAGTGAGATGTAT
E R H I P S H F Q K F R R S S A S E M Y
500 510

3541 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3600
CCAAAACTACAGAAGAACTGTGATCCGTCCTGAAGACTTCCCAAAGTTCATGCAATTG
P K T T E E T V I R P E D F P K F M Q L
520 530

3601 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3660
CACCAGAAATTTCTATGACTCCCTCAAAAATTTTGCATGCTGTTAAAACCTATCGTGTACA
H Q K F Y D S L K N F A C C *
540

ATATTGCCTGTATATTCCCCTCGAAATACGTTTATACTTTTTTCGCACGAGTTTTCTCAT

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997
Serial No.: 08/984,178
Customer No.: 21559
Page 4 of 23



5/23
FIG. 1E

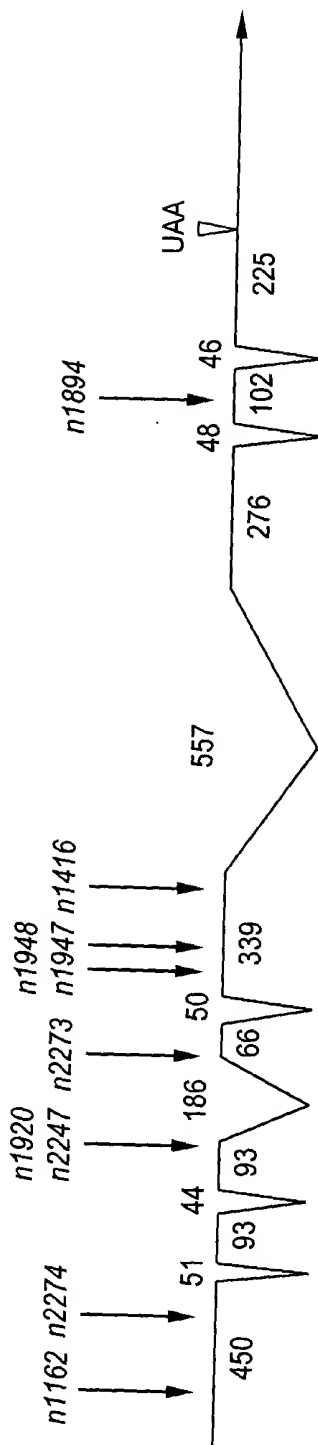
3661 -----+-----+-----+-----+-----+-----+-----+ 3720
TTTTCAATTTGTAATGTTTTATTTCTCTCCAAAATTTTCAGATCTATCCCAAATGTTCTTA
3721 -----+-----+-----+-----+-----+-----+-----+ 3780
AATTTAATGTTTTCTACAGATACTCAACACATCTTGTTTCATCTCATCCTTGCTTTTTTTT
3781 -----+-----+-----+-----+-----+-----+-----+ 3840
TTTCAAATATATTCAAGTTCTTTTATAATTTTAATTAATCGAATTAATACATTCACGTAA
3841 -----+-----+-----+-----+-----+-----+-----+ 3900
AGAATTTTCGTGGACTATTATTTTATCGCATCCAAATGATTTATTCCCTATTGTTTCGAAAC
3901 -----+-----+-----+-----+-----+-----+-----+ 3960
TTCCAAATTGATCATTTTTTAAACACGCCTCATTAATGAAAGTCGTACTTTTAGTCTCG
3961 -----+-----+-----+-----+-----+-----+-----+ 4020
AACATGAAGTAAGTTATTTTCTGTGTTCTAAATTCAAAGTGCATTCCAAAAGGACATTTG
4021 -----+-----+-----+-----+-----+-----+-----+ 4080
ATGAGTTTTTACGAAAACCGTAATTTTACAATTTCTTTTCAAGTGTTCGAT
4081 -----+-----+-----+-----+-----+-----+-----+ 4140
TTCTTTCTCTGTTGGCGTCATTACTACATTTGCTTTGCTGCTTCACTTTATCGAGATTC
4141 -----+-----+-----+-----+-----+-----+-----+ 4200
TTGCCATCAATGGAGTTCCATCTAGACCGATAGCAGTCTTCATATCATTATCCCTGTATA
4201 -----+-----+-----+-----+-----+-----+-----+ 4260
TTGTAATGTTTCAAGTATTTTAACTTATCGATTACGTACTATATTCAAGTGGTTCACTGTTT
4261 -----+-----+-----+-----+-----+-----+-----+ 4320
TCGGTCAATGGGTGACACGTGCTCGACGANNNAATTTTCAACGAACGCAATCTCCTAGTCA
4320 -----+-----+-----+-----+-----+-----+-----+ 4380
CTTATCAACCAAGAGCCCTCACCCATG
4380 -----+-----+-----+-----+-----+-----+-----+ 4407

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997
Page 5 of 23
Serial No.: 08/984,178
Customer No.: 21559

6/23

Title: CLONING, SEQUENCING AND CHARACTERIZATION
 OF TWO CELL DEATH GENES AND USES THEREFOR
 Applicant (s): H. Robert Horvitz et al.
 Filing Date: December 3, 1997 Serial No.: 08/984,178
 Page 6 of 23 Customer No.: 21559

FIG. 2





Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR

Applicant (s): H. Robert Horvitz et al.

Filing Date: December 3, 1997 Serial No.: 08/984,178

Page 7 of 23

Customer No.: 21559

7/23

FIG. 3

	10	12	14	18	21
	X	Y	Z	-X	-Z
	D	N	S	T	E
Calcium-binding loop consensus		D	N	S	
			D	E	
				Q	
				D	
				N	
EF-hand consensus	O	*	O	*	O
	G	*	*	O	*
	*	*	E		
ced-4 sequence 1	<u>Y</u>	N	N	Q	S
	H	L	A	D	F
	L	E			
sequence 2	<u>S</u>	L	<u>E</u>	I	D
	<u>E</u>	C	Y	D	F
	L	E			
Parvalbumin (carp)	D	Q	D	K	S
	G	F	I	E	E
	D	E			
(hake)	D	Q	D	K	D
	D	F	I	G	E
	D	E			
(ray)	D	S	D	G	D
	H	K	I	G	V
	D	E			
SCBP (<i>Amphioxus I</i>)	D	I	N	K	D
	D	V	V	S	W
	E	E			
ICaBP (bovine)	A	K	E	G	D
	P	Q	L	S	K
	E	E			
	D	K	N	G	D
	G	E	V	S	F
	E	E			
Troponin C (rabbit)	D	A	D	G	G
	G	D	I	S	V
	K	E			
	D	E	D	G	S
	G	T	I	D	F
	E	E			
	D	R	N	A	D
	G	Y	I	D	A
	E	E			
	D	K	N	N	D
	G	R	I	D	F
	D	E			
Calmodulin (bovine)	D	K	D	G	N
	G	T	I	T	T
	K	E			
Trypsinogen	L	G	E	D	N
	I	N	V	E	G
	N	E			
Fibrinogen	D	N	D	N	D
	K	F	E	G	N
	C	A	E		
Villin	G	V	D	P	S
	R	K	E	N	H
	L	S			
GBP	D	L	N	K	D
	G	Q	I	Q	_
	I	E			

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Customer No.: 21559
Page 8 of 23



9/23
FIG. 4B

-----> Repeat 1
<-----
TGTAGCGCTTGTGTCGATTTACGGGCTCAATTTTTGAAAATAATTTTTTTTTTCGAATTT
1441 -----+-----+-----+-----+-----+-----+ 1500

TGATAACCCGTAAATCGTCACAACGCTACAGTAGTCATTTAAAGGATTACTGTAGTTCTA
1501 -----+-----+-----+-----+-----+-----+ 1560

GCTACGAGATATTTTGC GCGCCAAATATGACTGTAATACGCATTCTCTGAATTTTGTGTT
1561 -----+-----+-----+-----+-----+-----+ 1620
TCCGTAATAATTTT CACAAGATTTTGGCATTCCACTTTAAAGGCGCACAGGATTTATTCCA
1621 -----+-----+-----+-----+-----+-----+ 1680
ATGGGTCTCGGCACGCAAAAAGTTTGATAGACTTTTAAATTCTCCTTGCAATTTTAAATTC
1681 -----+-----+-----+-----+-----+-----+ 1740
AATTACTAAAATTTTCTGTAATTTTCTGTTAAATTTTAAATCAGTTTTCTAATATT
1741 -----+-----+-----+-----+-----+-----+ 1800
TTCCAGGCTGACAAACAGAAACAAAAACACAACAAACATTTTAAAAATCAGTTTTCAAT
1801 -----+-----+-----+-----+-----+-----+ 1860
TAAAAATAACGATTTCTCATTGAAAATTGTGTTTATGTTTGC GAAAATAAAAGAGAACT
1861 -----+-----+-----+-----+-----+-----+ 1920
GATTCAAAACAATTTTAA CAAAAAAACCCCAAAATTCGCCAGAAATCAAGATAAAAAA
1921 -----+-----+-----+-----+-----+-----+ 1980
TTCAAGAGGGTCAAAATTTTCCGATTTTACTGACTTTCACCTTTTTTTTCGTAGTTCAGT
1981 -----+-----+-----+-----+-----+-----+ 2040
GCAGTTGTTGGAGTTTTTGACGAAACTAGGAAAAAATCGATAAAAAATTACTCAAATCG
2041 -----+-----+-----+-----+-----+-----+ 2100
AGCTGAATTTTGAGGACAATGTTTAAAAAAAACACTATTTTCCAATAATTTCACTCAT
2101 -----+-----+-----+-----+-----+-----+ 2160

TTTCAGACTAAATCGAAAATCAAATCGTACTCTGACTACGGGTCAGTAGAGAGGTCAACC

2161 -----+-----+-----+-----+-----+-----+ 2220

ATCAGCCGAAGATGATGCGTCAAGATAGAAGGAGCTTGCTAGAGAGGAACATTATGATGT
2221 -----+-----+-----+-----+-----+-----+ 2280
M M R Q D R R S L L E R N I M M F
1 10
T (n1040)
|
TCTCTAGTCATCTAAAAGTCGATGAAATTCTCGAAGTTCTCATCGCAAAACAAGTGTGTA
2281 -----+-----+-----+-----+-----+-----+ 2340
S S H L K V D E I L E V L I A K Q V L N
20 30
| Intron 1
ATAGTGATAATGGAGATATGATTAATGTGAGTTTTTAATCGAATAATAATTTTAAAAAAA
2341 -----+-----+-----+-----+-----+-----+ 2400
S D N G D M I N
40

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997
Page 9 of 23
Serial No.: 08/984,178
Customer No.: 21559



10/23

FIG. 4C

AATTGATAATATAAAGAATATTTTTGCAGTCATGTGGAACGGTTCGCGAGAAGAGACGGG
2401 -----+-----+-----+-----+-----+-----+-----+ 2460
S C G T V R E K R R E
50
A (n718)
AGATCGTGAAAGCAGTGCAACGACGGGGAGATGTGGCGTTCGACGCGTTTTATGATGCTC
2461 -----+-----+-----+-----+-----+-----+ 2520
I V K A V Q R R G D V A F D A F Y D A L
60 70
| Intron 2
TTCGCTCTACGGGACACGAAGGACTTGCTGAAGTTCTTGAACCTCTCGCCAGATCGTAGG
2521 -----+-----+-----+-----+-----+-----+ 2580
R S T G H E G L A E V L E P L A R S
80 90
TTTTTAAAGTTCGGCGCAAAGCAAGGGTCTCACGGAAAAAGAGGCGGATCGTAATTTT
2581 -----+-----+-----+-----+-----+-----+ 2640
GCAACCCACCGGCACGGTTTTTTTCTCCGAAAATCGGAAATTATGCACTTTCCCAAATAT
2641 -----+-----+-----+-----+-----+-----+ 2700
TTGAAGTGAAATATATTTTATTTACTGAAAGCTCGAGTGATTATTTATTTTAACTA
2701 -----+-----+-----+-----+-----+-----+ 2760
ATTTTCGTGGCGCAAAGGCCATTTTGTAGATTGCGCGAAAATACTTGTCACACACACAC
2761 -----+-----+-----+-----+-----+-----+ 2820
ACACACATCTCCTTCAAATATCCCTTTTTTCCAGTGTGACTCGAATGCTGTGCAATTGCA
2821 -----+-----+-----+-----+-----+-----+ 2880
V D S N A V E F E
100
GTGTCCAATGTCACCGGCAAGCCATCGTCGGAGCCGCGCATTGAGCCCCGCGGCTACAC
2881 -----+-----+-----+-----+-----+-----+ 2940
C P M S P A S H R R S R A L S P A G Y T
110 120
TTCACCGACCCGAGTTCACCGTGACAGCGTCTCTTCAGTGTTCATTCACCTTCTTATCA
2941 -----+-----+-----+-----+-----+-----+ 3000
S P T R V H R D S V S S V S S F T S Y Q
130 140
GGATATCTACTCAAGAGCAAGATCTCGTTCTCGATCGCGTGCACTTCATTCATCGGATCG
3001 -----+-----+-----+-----+-----+-----+ 3060
D I Y S R A R S R S R S R A L H S S D R
150 160
| Intron 3
ACACAATTATTCATCTCCTCCAGTCAACGCATTTCCAGCCAACCTTGTATGTTGATGCG
3061 -----+-----+-----+-----+-----+-----+ 3120
H N Y S S P P V N A F P S Q P S
170

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Customer No.: 21559
Page 10 of 23

11/23
FIG. 4D

Repeat 1

```

-----
AACACTAAATTCTGAGAAATGCGCATTACTCAACATATTTGACGCGCAAATATCTCGTAGC
3121 -----+-----+-----+-----+-----+-----+ 3180
-----
GAAAAATACAGTAACCCCTTTAAATGACTATTGTAGTGTGATTACGGGCTCGATTTTCG
3181 -----+-----+-----+-----+-----+-----+ 3240
-->
AAACGAATATATGCTCGAATTGTGACAACGAATTTTAATTTGTCATTTTGTGTTTTCTT
3241 -----+-----+-----+-----+-----+-----+ 3300

```

Repeat 1

```

-----
TTGATATTTTTGATCAATTAATAAATTATTTCCGTAAACAGACACCAGCGCTACAGTACT
3301 -----+-----+-----+-----+-----+-----+ 3360
-----
CTTTTAAAGAGTTACAGTAGTTTTTCGCTTCAAGATATTTTGAAAAGAATTTTAAACATTT
3361 -----+-----+-----+-----+-----+-----+ 3420
TGAAAAAAAAATCATCTAACATGTGCCAAAACGCTTTTTTCAAGTTTCGCAGATTTTTTGA
3421 -----+-----+-----+-----+-----+-----+ 3480

```

Repeat 2

```

-----
TTTTTTTCATTCAAGATATGCTTATTAACACATATAATTATCATTAATGTGAATTTCTTG
3481 -----+-----+-----+-----+-----+-----+ 3540
-----
TAGAAATTTTGGGCTTTTCGTTCTAGTATGCTCTACTTTTGAAATTGCTCAACGAAAAAA
3541 -----+-----+-----+-----+-----+-----+ 3600
-----
TCATGTGGTTTGTTTCATATGAATGACGAAAAATAGCAATTTTTTATATATTTTCCCCTAT
3601 -----+-----+-----+-----+-----+-----+ 3660
-----
TCATGTTGTGCAGAAAAATAGTAAAAAAGCGCATGCATTTTTCGACATTTTTCATCGA
3661 -----+-----+-----+-----+-----+-----+ 3720
----->
ACGACAGCTCACTTCACATGCTGAAGACGAGAGACGCGGAGAAATACCACACATCTTTCT
3721 -----+-----+-----+-----+-----+-----+ 3780

```

Repeat 2

```

-----
GCGTCTCTCGTCTTCAGCATGTGAAATGGGATCTCGGTCGATGTAAAAAATGTCGAATA
3781 -----+-----+-----+-----+-----+-----+ 3840
-----
ATGTAAAAAATGCATGCGTTTTTTTTACACTTTTCTGCACAAATGAATAGGGGGAAAAATGT
3841 -----+-----+-----+-----+-----+-----+ 3900

```



12/23
FIG. 4E

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997
Page 12 of 23
Serial No.: 08/984,178
Customer No.: 21559

```
-----
ATTAAAATACATTTTTTGTATTTTTCAACATCACATGATTAACCCCATTTATTTTTTCGTT
3901 -----+-----+-----+-----+-----+-----+ 3960

-----
GAGCAACTTAAAAAGTAGAGAATATTAGAGCGAAAACCAAATTTCTTCAAGATATTACC
3961 -----+-----+-----+-----+-----+-----+ 4020

-----
TTTATTGATAATTATAGATGTTAATAAGCATATCTTGAATGAAAGTCAGCAAAAATATGT
4021 -----+-----+-----+-----+-----+-----+ 4080
GCGAAACACCTGAAAAAATCAAAAATCTGCGAAAATTGAAAAATGCATTAAAAATACA
4081 -----+-----+-----+-----+-----+-----+ 4140
TTTTTGCATTTTCTACATCACATGAATGTAGAAAATTAAAAGGGAAATCAAAATTTCTA
4141 -----+-----+-----+-----+-----+-----+ 4200
GAGGATATAATTGAATGAAACATTGCGAAATTAAAATGTGCGAAACGTCAAAAAAGAGGA
4201 -----+-----+-----+-----+-----+-----+ 4260

-----
AATTTGGGTATCAAAATCGATCCTAAAACCAACACATTTTCAGCATCCGCCAACTCTTCAT
4261 -----+-----+-----+-----+-----+-----+ 4320
                                     S A N S S F
                                     180

-----
TCACCGGATGCTCTTCTCTCGGATACAGTTCAAGTCGTAATCGCTCATTTCAGCAAAGCTT
4321 -----+-----+-----+-----+-----+-----+ 4380
    T G C S S L G Y S S S R N R S F S K A S
    190                                200

-----
CTGGACCAACTCAATACATATTCCATGAAGAGGATATGAACTTTGTGCGATGCACCAACCA
4380 -----+-----+-----+-----+-----+-----+ 4440
    G P T Q Y I F H E E D M N F V D A P T I
    210                                220

-----
TAAGCCGTGTTTTTCGACGAGAAAAACCATGTACAGAACTTCTCGAGTCCTCGTGGAATGT
4441 -----+-----+-----+-----+-----+-----+ 4500
    S R V F D E K T M Y R N F S S P R G M C
    230                                240

-----
GCCTCATCATAAATAATGAACACTTTGAGCAGATGCCAACACGGAATGGTACCAAGGCCG
4501 -----+-----+-----+-----+-----+-----+ 4560
    L I I N N E H F E Q M P T R N G T K A D
    250                                260

-----
ACAAGGACAATCTTACCAATTTGTTTCAGATGCATGGGCTATACGGTTATTTGCAAGGACA
4561 -----+-----+-----+-----+-----+-----+ 4620
    K D N L T N L F R C M G Y T V I C K D N
    270                                280

-----
| Intron 4
ATCTGACGGGAAGGGTACGGCGAAATTATATTACCCAAACGCGAAATTTGCCATTTTGCG
4621 -----+-----+-----+-----+-----+-----+ 4680
    L T G R
```

13/23
FIG. 4F

Repeat 3

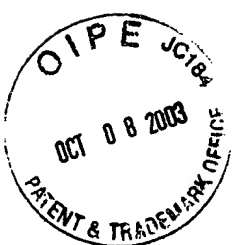
----->
CCGAAAATGTGGCGCCCGGTCTCGACACGACAATTTGTGTAAATGCAAAAATGTATAAT
4681 -----+-----+-----+-----+-----+-----+ 4740
TTTGCAAAAAACAAAATTTTGAACCTCCGCGAAAATGATTTACCTAGTTTCGAAATTTTC
4741 -----+-----+-----+-----+-----+-----+ 4800
GTTTTTTCGGCTACATTATGTGTTTTTCTTAGTTTTTCTATAATATTTGATGTAAAAA
4801 -----+-----+-----+-----+-----+-----+ 4860
ACCGTTTGTAATTTTCAGACAATTTTCCGCATACAAAACCTTGATAGCACGAAATCAATT
4861 -----+-----+-----+-----+-----+-----+ 4920
TTCTGAATTTTCAAAATTTATCCAAAAATGCACAATTTAAAATTTGTGAAAATTGGCAAAC
4921 -----+-----+-----+-----+-----+-----+ 4980
GGTGTTCATATGAAATGTATTTTAAAAACTTTAAAAACCACTCCGAAAAGCAATAA
4981 -----+-----+-----+-----+-----+-----+ 5040
AAATCAAAAACACGTCACAATTCAAATTCAAAAGTTATTCATCCGATTTGTTTATTTTG
5041 -----+-----+-----+-----+-----+-----+ 5100
CAAAATTTGAAAAATCATGAAGGATTTAGAAAAAGTTTATAACATTTTCTAGATTTT
5101 -----+-----+-----+-----+-----+-----+ 5160
TCAAAATTTTTTTTAAACAATCGAGAAAAAGAGAATGAAAAATCGATTTTAAAAATATCC
5161 -----+-----+-----+-----+-----+-----+ 5220

Repeat 3

<-----
ACAGCTTCGAGAGTTTGAAATTACAGTACTCCTTAAAGGCGCACACCCCATTTGCATTGG
5221 -----+-----+-----+-----+-----+-----+ 5280

ACCAAAAATTTGTCGTGTCGAGACCAGGTACCGTAGTTTTTGTGCGAAAAATTGCACCAT
5281 -----+-----+-----+-----+-----+-----+ 5340
TGGACAATAAACCTTCCTAATCACCAAAAAGTAAAATTGAAATCTTCGAAAAGCCAAAAA
5341 -----+-----+-----+-----+-----+-----+ 5400
ATTCAAAAAAAAAGTCGAATTTTCGATTTTTTTTTTTGGTTTTTGGTCCCAAAAACCAAAA
5401 -----+-----+-----+-----+-----+-----+ 5460
AAATCAATTTTTCGAAAATACCAAAAAGAAACCCGAAAAAATTTCCAGCCTTGTTCTT
5461 -----+-----+-----+-----+-----+-----+ 5520
|
AATGTAAACTGATATTTAATTTCCAGGGAATGCTCCTGACAATTCGAGACTTTGCCAAAC
5521 -----+-----+-----+-----+-----+-----+ 5580
G M L L T I R D F A K H
290 300
ACGAATCACACGGAGATTCTGCGATACTCGTGATTCTATCACACGGAGAAGAGAATGTGA
5581 -----+-----+-----+-----+-----+-----+ 5640
E S H G D S A I L V I L S H G E E N V I
310 320
TTATTGGAGTTGATGATATACCGATTAGTACACACGAGATATATGATCTTCTCAACGCGG
5641 -----+-----+-----+-----+-----+-----+ 5700
I G V D D I P I S T H E I Y D L L N A A
330 340

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Customer No.: 21559
Page 13 of 23



14/23
FIG. 4G

A (n2433)
| Intron 5
CAAAATGCTCCCCGTCTGGCGAATAAGCCGAAAATCGTTTTTGTGCAGGCTTGTTCGAGGCG
5701 -----+-----+-----+-----+-----+ 5760
N A P R L A N K P K I V F V Q A C R G E
350 360
|
GTTTCGTTTTTTATTTTAATTTTAATATAAAATATTTTAAATAAAATTCATTTTCAGAACGTC
5761 -----+-----+-----+-----+-----+ 5820
R R
GTGACAATGGATTCCCAGTCTTGGATTCTGTGCACGGAGTTCCTGCATTTCTTCGTCGTG
5821 -----+-----+-----+-----+-----+ 5880
D N G F P V L D S V D G V P A F L R R G
370 380
T (n1165)
|
GATGGGACAATCGAGACGGGCCATTGTTCAATTTTCTTGGATGTGTGCGGCCGCAAGTTC
5881 -----+-----+-----+-----+-----+ 5940
W D N R D G P L F N F L G C V R P Q V Q
390 400
| Intron 6
AGGTTGCAATTTAATTTCTTGAATGAGAATATTCCTTCAAAAAATCTAAAAATAGATTTTT
5941 -----+-----+-----+-----+-----+ 6000
ATTCCAGAAAGTCCCGATCGAAAAATTGCGATATAATTACGAAATTTGTGATAAAATGAC
6001 -----+-----+-----+-----+-----+ 6060
Repeat 4

AAACCAATCAGCATCGTCGATCTCCGCCCAC TTCGGAATTGGTTTGAAAAGTGGGCGGA
6061 -----+-----+-----+-----+-----+ 6120
----->-----
GTGAATTGCTGATTGGTCGCAGTTTTTCAGTTTAGAGGGAATTTAAAAATCGCCTTTTCGA
6121 -----+-----+-----+-----+-----+ 6180
AAATTAAAAATTGATTTTTTTCAATTTTTTCGAAAAATATTCGGATTATTTTATATTCCTT
6181 -----+-----+-----+-----+-----+ 6240
A (n717)
|
GGAGCGAAAGCCCCGTCTGTAAACATTTTTTAAATGATAATTAATAAAATTTTGCAGCAA
6241 -----+-----+-----+-----+-----+ 6300
Q
T (n1949)
|
GTGTGGAGAAAGAAGCCGAGCCAAGCTGACATTCTGATTTCGATACGCAACGACAGCTCAA
6301 -----+-----+-----+-----+-----+ 6360
V W R K K P S Q A D I L I R Y A T T A Q
410 420

15/23
FIG. 4H

A (n1286)

6361 TATGTTTCGTGGAGAAACAGTGTCTCGTGGATCATGGTTCATTCAAGCCGTCTGTGAAGTG 6420
-----+-----+-----+-----+-----+
Y V S W R N S A R G S W F I Q A V C E V
430 440

T (n1129, n1164)

6421 TTCTCGACACACGCAAAGGATATGGATGTTGTTGAGCTGCTGACTGAAAGTCAATAAGAAG 6480
-----+-----+-----+-----+-----+
F S T H A K D M D V V E L L T E V N K K
450 460

T (n2430)

A (n2426)

6481 GTCGCTTGTGGATTTTCAGACATCACAGGGATCGAATATTTTGAAACAGATGCCAGAGGTA 6540
-----+-----+-----+-----+-----+
V A C G F Q T S Q G S N I L K Q M P E
470 480
Intron 7

Repeat 5

6541 CTTGAAACAAACAATGCATGTCTAACTTTTAAGGACACAGAAAAATAGGCAGAGGCTCCT 6600
-----+-----+-----+-----+-----+
----->
6601 TTTGCAAGCCTGCCGCGCGTCAACCTAGAATTTTAGTTTTCTAGCTAAAAATGATTGATTTT 6660
-----+-----+-----+-----+-----+
6661 GAATATTTTATGCTAATTTTTTTGCGTTAAATTTTGAAATAGTCACTATTTATCGGGTTT 6720
-----+-----+-----+-----+-----+
6721 CCAGTAAAAAATGTTTATTAGCCATTGGATTTTACTGAAAAACGAAAAATTTGTAGTTTTTC 6780
-----+-----+-----+-----+-----+
6781 AACGAAATTTATCGATTTTTTAAATGTAAAAAATAAGCGAAAAATTACATCAACCATCAA 6840
-----+-----+-----+-----+-----+
6841 GCATTTAAGCCAAAATTGTAACTCATTTAAAAATTAATTCAAAGTTGTCCACGAGTATT 6900
-----+-----+-----+-----+-----+

Repeat 5

6901 ACACGGTTGGCGCGCGCAAGTTTGCAAAACGACGCTCCGCCTCTTTTCTGTGCGGCTT 6960
-----+-----+-----+-----+-----+

T (n1163)

6961 GAAAACAAGGGATCGGTTTAGATTTTTTCCCCAAAATTTAAATTAAATTCAGATGACATC 7020
-----+-----+-----+-----+-----+
M T S

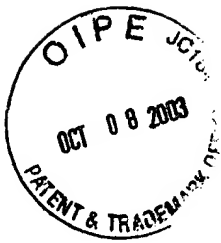
7021 CCGCCTGCTCAAAAAGTTCTACTTTTTGGCCGGAAGCACGAAACTCTGCCGTCTAAATTC 7080
-----+-----+-----+-----+-----+
R L L K K F Y F W P E A R N S A V *
490 500



16/23

FIG. 4I

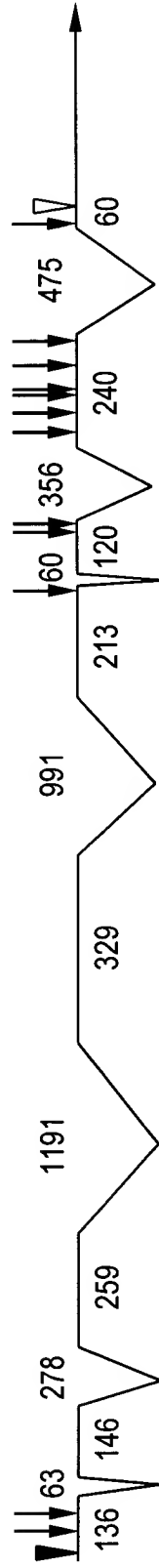
```
ACTCGTGATTCATTGCCCAATTGATAATTGTCTGTATCTTCTCCCCAGTTCTCTTTCGC
7081 -----+-----+-----+-----+-----+-----+ 7140
CCAATTAGTTTAAAACCATGTGTATATTGTTATCCTATACTCATTTCACTTTATCATTCT
7141 -----+-----+-----+-----+-----+-----+ 7200
ATCATTTCCTTCCCATTTTCACACATTTCCATTTCTCTACGATAATCTAAAATTATGAC
7201 -----+-----+-----+-----+-----+-----+ 7260
GTTTGTGTCTCGAACGCATAATAATTTTAATAACTCGTTTGAATTTGATTAGTTGTTGT
7261 -----+-----+-----+-----+-----+-----+ 7320
GCCCAGTATATATGTATGTACTATGCTTCTATCAACAAAATAGTTTCATAGATCATCACC
7321 -----+-----+-----+-----+-----+-----+ 7380
CCAACCCACCAACCTACCGTACCATATTCATTTTTGCCGGAATCAATTCGATTAATT
7381 -----+-----+-----+-----+-----+-----+ 7440
TTAACCTATTTTTTCGCCACAAAAATCTAATATTTGAATTAACGAATAGCATTCATC
7441 -----+-----+-----+-----+-----+-----+ 7500
TCTCCCGTGCCGGAATGCCTCCCGGCCTTTTAAAGTTCGGAACATTTGGCAATTATGTAT
7501 -----+-----+-----+-----+-----+-----+ 7560
AAATTTGTAGGTCCCCCATCATTTCCCGCCCATCATCTCAAATTGCATTCTTTTTTCG
7561 -----+-----+-----+-----+-----+-----+ 7620
CCGTGATATCCCGATTCTGGTCAGCAAAGATCT
7621 -----+-----+-----+-----+-----+ 7653
```

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Page 17 of 23 Customer No.: 21559

FIG. 5A

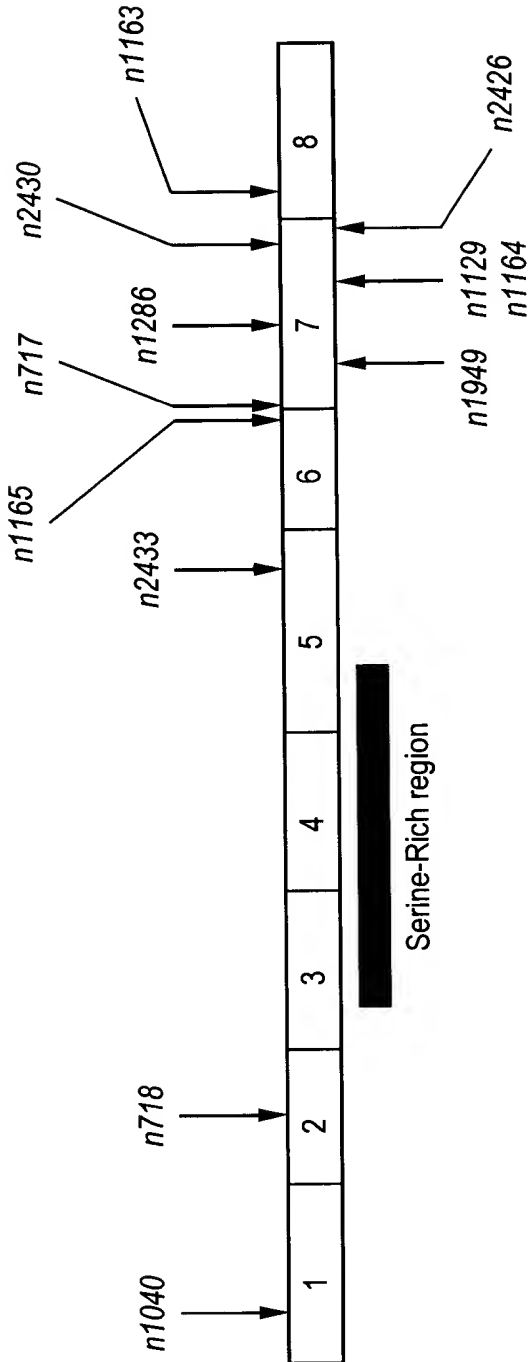
17/23



Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Page 18 of 23 Customer No.: 21559

FIG. 5B

ced-3 Mutations are Clustered

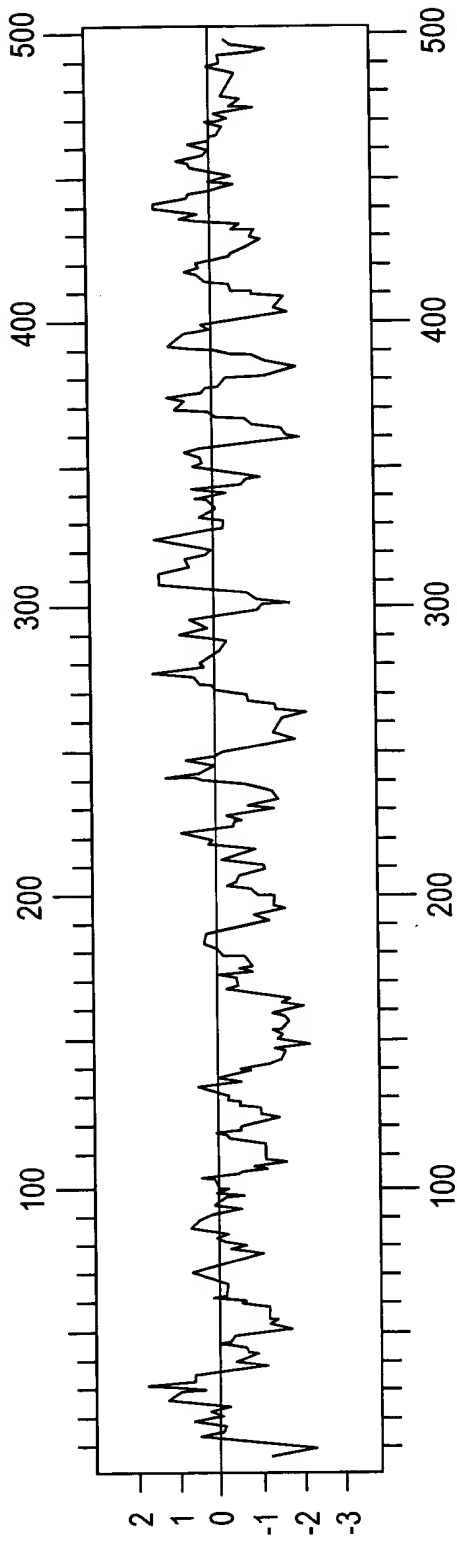




Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Page 19 of 23 Customer No.: 21559

19/23

FIG. 6





20/23
FIG. 7

Lines

1 01 MMRQDRRSLLERNIMMFSSHLKVDEILEVLIQVLNSDNGDMINSCGTV 50
2W.....LE...K.QA.L..D.....V....R.E
3 TVS.SLI..R..... M.....

1 51 REKRREIVKAVQRPQDVAFDAFYDALRSTGHEGLAEVLEPLARSVDNAV 100
2 .DNEK.....R..E.....D...ND..D..M..S.P .P.
3

1 101 EFECPMSPASHRRSRALSPAGYTSPTRVHRDSVSSVSFTS YQDIYSRA 149
2 PM.....S.....P .A.....I.....T...V....
3 S

1 150 RSRSR SRALHSSDRHNYSSPPVNAFPPSQSSANSSTGCSLGYSSRN 198
2 ..S..S..P.Q.....M.AA_TS.....A.....
3 T..._.P..T.....V..S_.S.Q...A.....S.....T

1 199 RSFSKASGPTQYIFHEEDMNFVDAPTISRVDKTYRNFSSPRGMCLI 247
2T.AQS.....Y.....H.....L...
3 ..Y....AHS.....Y.....H.....T...L...

1 248 INNEHFQMPTRNGTKADKDNLTNLFRMGYTVICKDNLTGRGMLLTIRD 297
2I.....E..S...S
3P...IS.....I.H.....M.....

1 298 FAKHESHGDSAILVILSHGEENVIGVDDIPSTHEIYDLLNAANAPRLA 347
2 .GRNDM.....VSVNV.....
3 ...N.T.....VSVNV...X.....

1 348 NKPKIVFVQACRGERRDNGFPVLDSVDGVPFLRRGWDNRDGPLFNFLGC 397
2L.....SLI.....
3L.....V.....LI....KG... ..

1 398 VRPQVQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFIQAVCEVFST 447
2M..A.....L
3A.....A.....L

1 448 HAKMDVVELLTEVNKKVACGFQTSQGSNILKQMPEMTSRLLKKFYFWPE 497
2L.....
3A.....L.....

1 498 _ARN_SAV 503
2 DRG..._
3 _D..RS...

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Page 20 of 23 Customer No.: 21559

Line 1 C. elegans
Line 2 C. briggsae
Line 3 C. vulgaris

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Page 21 of 23 Customer No.: 21559

FIG. 8

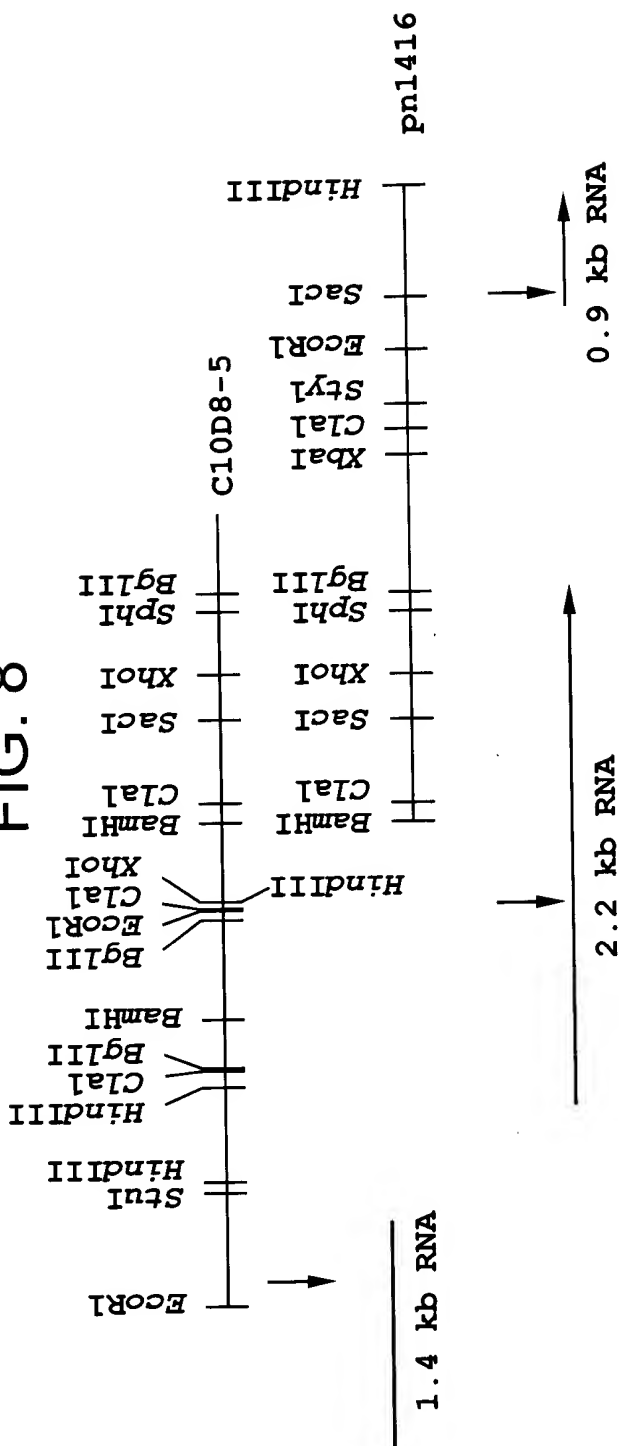
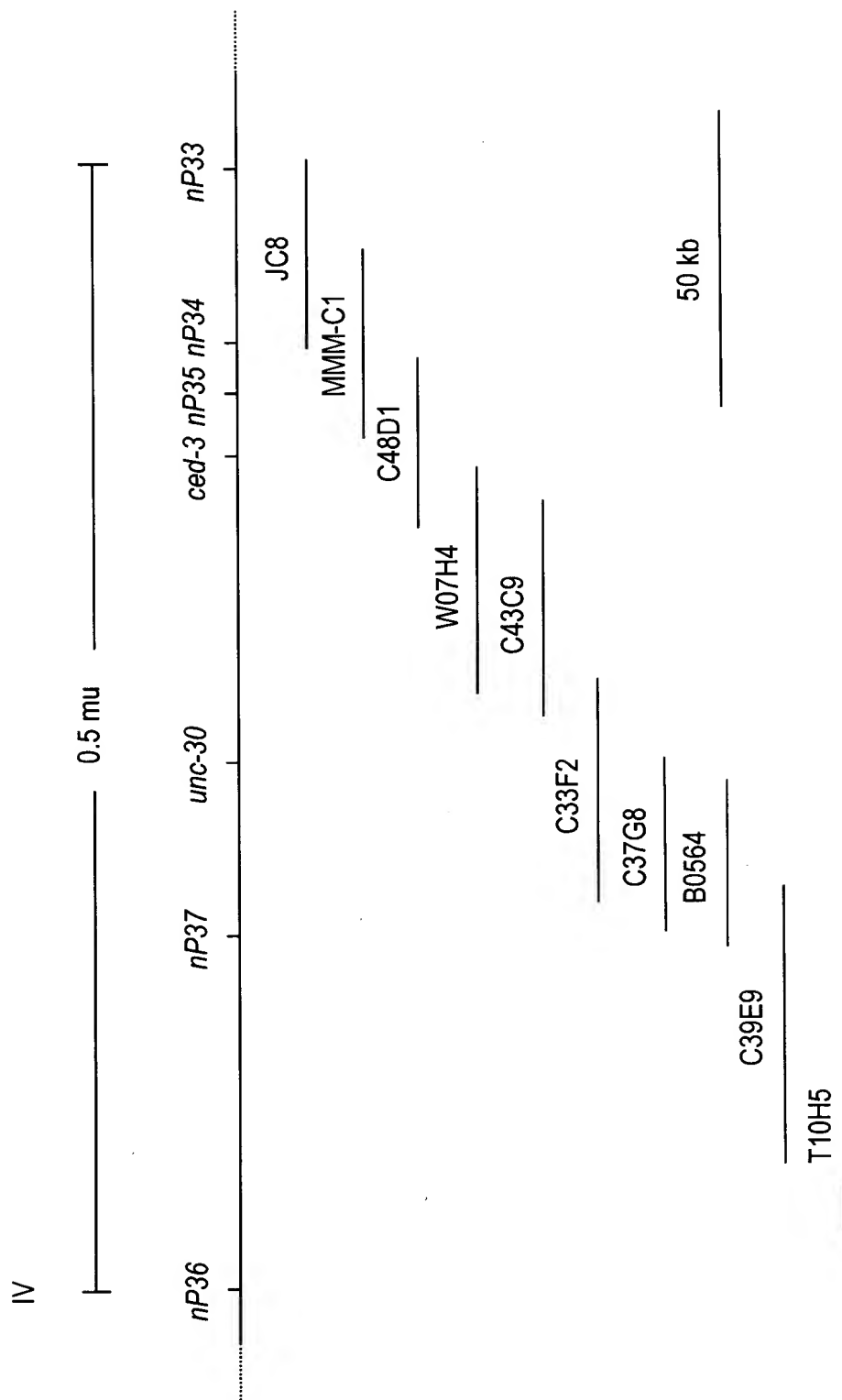


FIG. 9





Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997 Serial No.: 08/984,178
Page 23 of 23 Customer No.: 21559

FIG. 10

Summary of the experiments to localize *ced-3* gene within C40D1

DNA	5kb		<i>ced-3</i> activity	No. lines
C48D1	BamHI	BamHI	++	2
C48D1-20	BamHI	BamHI BglII BglII Apal BglII BglII	++	2
C48D1-43	BamHI	BamHI BglII BglII Apal BglII	++	1
pJ40	BamHI	BamHI BglII BglII Apal	++	1
pJ107	BamHI	BamHI BglII BglII	++	1
pJ107del28 & pJ107del34		BglII BglII	++	3
pJ107del12 & pJ107del27		BglII BglII	+	1
pJ55 & pJ56	BamHI	BamHI BglII Sall	-	12